FIG.1

GACCGGCTGCCCCGCCTGGAGGAGATCCGCATCTGGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTTACAGGCGGTATGGCGAGGAGTATGGCAACCTCACCCGCCCAGACA
TCACCTTCACCTACTTCCAGCCTAAGCCACGGCAGGCCTGGGTGTGGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGGCAGGGCTGCGCTGGGTAAACTACAGCTGCCTG
GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCCTGCGTGCTCGAACCCTGCCCTCCCTACTGGGCGGTGGGA
GACTTCGGCCCATGCAGCGCCTCCTGTGGGGGTGGCCTGCGGGAGCGGCCAGTGCGC
TGCGTGGAGGCCCAGGGCAGCCTCCTGAAGACATTGCCCCCAGCCCGGTGCAGAGCA
GGGGCCCAGCAGCCAGCTGTGGCGCTGGAAACCTGCAACCCCCAGCCCTGCCCTGCC
AGGTGGAGGTGTCAGAGCCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGGCAGATGGCCTGGAGGCTCCAGTGACTGAGG
GGCCTGGCTCCGTAGATGAGAAGCTGCCTGCCCCTGAGCCCTGTGTCGGGATGTCATG
TCCTCCAGGCTGGGGCCATCTGGATGCCACCTCTGCAGGGGAGAAGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGGCTCAAGCTGCACACGTGTGGACCCCTGCGGCAGGG
TCGTGCTCCGTCTCCTGCGGGCGAGGTCTGATGGAGCTGCGTTTCCTGTGCATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGGCCTGGCAAGCAAGCCTGGGAG
CCGGCGGGAGGTCTGCCAGGCTGTCCCGTGCCCTGCTCGGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGGAGAGGGGTCGTGCGGAGGATCCTGTATTGTGCCCG
GGCCCATGGGGAGGACGATGGTGAGGAGATCCTGTTGGACACCCAGTGCCAGGGGCT
GCCTCGCCCGGAACCCCAGGAGGCCTGCAGCCTGGAGCCCTGCCCACCTAGGTGGAA
AGTCATGTCCCTTGGCCCATGTTCGGCCAGCTGTGGCCTTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCGGCCTGT
GCGGCGCTGGTGCGGCCCGAGGCCAGTGTCCCCTGTCTCATTGCCGACTGCACCTACC
GCTGGCATGTTGGCACCTGGATGGAGTGCTCTGTTTCCTGTGGGGATGGCATCCAGCG
CCGGCGTGACACCTGCCTCGGACCCCAGGCCCAGGCGCCTGTGCCAGCTGATTTCTGC
CAGCACTTGCCCAAGCCGGTGACTGTGCGTGGCTGCTGGGCTGGGCCCTGTGTGGGAC
AGGGTACGCCCAGCCTGGTGCCCCACGAAGAAGCCGCTGCTCCAGGACGGACCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCACCTTGAGCCAACAGGAACCATTGACAT
GCGAGGCCCAGGGCAGGCAGACTGTGCAGTGGCCATTGGGCGGCCCCTCGGGGAGGT
GGTGACCCTCCGCGTCCTTGAGAGTTCTCTCAACTGCAGTGCGGGGGACATGTTGCTG
CTTTGGGGCCGGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTTCA
GCTCCAAGACCAACACGCTGGTGGTGAGGCAGCGCTGCGGGCGGCCAGGAGGTGGGG
TGCTGCTGCGGTATGGGAGCCAGCTTGCTCCTGAAACCTTCTACAGAGAATGTGACATG
CAGCTCTTTGGGCCCTGGGGTGAAATCGTGAGCCCCTCGCTGAGTCCAGCCACGAGTA
ATGCAGGGGGCTGCCGGCTCTTCATTAATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCCATGGGCAGCAGGTGCTCTACTG

GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTCAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCGGGGCCAGTACTGGACCCTCCAATCATGGGTACCGGAGATGCAGGACC
CTCAGTCCTGGAAGGGAAAGGAAGGAACC

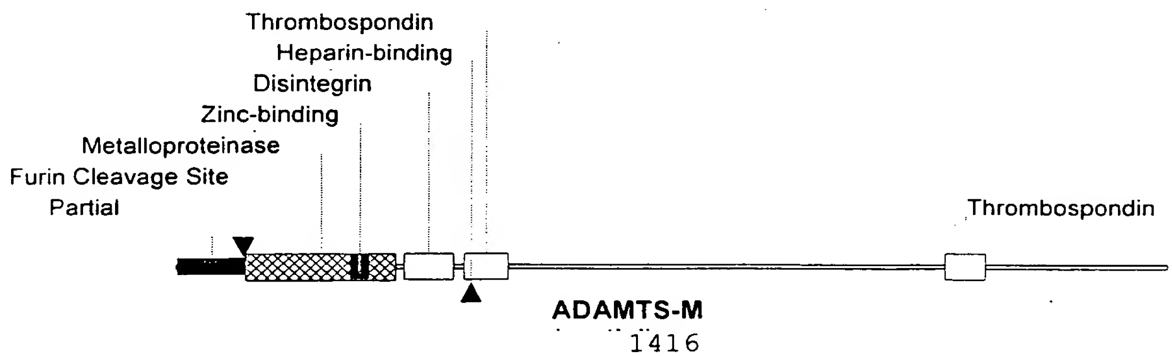
FIG. 2

PGRPTRPKAPSHSAPLLGLALLRMHQRHPRARCPPLCVAGILACGFLLGCWGPSHFQQSCL
QALEPQAVSSYLSPGAPLKGRPPSPGFQRQRQRRAAGGILHLELLVAVGPDVFQAHQED
TERYVLTNLNIGAELLRDPSLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCGWSQTINP
EDDTDPGHADLVLYITRFDLELPDGNRQVRGVTQLGGACSPTWSCLITEDTGFDLGVTIAHEI
GHSFGLEHDGAPGSGCGPSGHVMASDGAAPRAGLAWSPCSRRQLLSLLSAGRARCVWDP
PRPQPGSAGHPPDAQPGLYYSANEQCRVAFGPKAVACTFAREHLDMCQALSCHTDPLDQS
SCSRLLVPLLDGTECGVEKWCSKGRCRSLVELTPIAAVHGRWSSWGPRSPCSRSCGGGVV
TRRRQCNNPRPAFGGRACVGADLQAEMCNTQACEKTQLEFMSQQCARTDGQPLRSSPGG
ASFYHWGAAVPHSQGDALCRHMCRAIGESFIMKRGDSFLDGTRCMPSGPREDGTLSLCVS
GSCRTFGCDGRMDSQQVWDRCQVCGGDNSTCSPRKGSFTAGRAREYVTFLTVTPNLTSV
YIANHRPLFTHLAVRIGGRYVVAGKMSISPNTTYPSLLEDGRVEYRVALTEDRLPRLEEIRIWG
PLQEDADIQVYRRYGEEYGNLTRPDITFTYFQPKPRQAWVWAAVRGPCSVSCGAGLRWVN
YSCLDQARKELVETVQCQGSQQPPAWPEACVLEPCPPYWAVGDFGPCSASCGGGLRERP
VRCVEAQGSLLKTLPPARCRAGAQQPAVALETCNPQPCPARWEVSEPSSCTSAGGAGLAL
ENETCVPGADGLEAPVTEGPGSVDEKLPAPEPCVGMSCPPGWGHLDATSAGEKAPSPWG
SIRTGAQAAHVWTPAAGSCSVSCGRGLMELRFLCMDSALRVPVQEELCGLASKPGSRREV
CQAVPCPARWQYKLAACSVSCGRGVVRRILYCARAHGEDDGEEILLDTQCQGLPRPEPQE
ACSLEPCPPRWKVMSLGPCSASCGLGTARRSVACVQLDQGQDVEVDEAACAALVRPEASV
PCLIADCTYRWHVGTWMECSVSCGDGIQRRRDTCLGPQAQAPVPADFCQHLPKPVTVRGC
WAGPCVGQGTPSLVPHEEAAAPGRTTATPAGACGRQHLEPTGTIDMRGPGQADCAVAIGR
PLGEVVTLRVLESSLNCSAGDMLLLWGRLTWRKMCRKLLDMTFSSKTNTLVVRQRCGRPG
GGVLLRYGSQLAPETFYRECDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAIHAL
ATNMGAGTEGANASYILIRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRG
QYWTLQSWVPEMQDPQSWKGKEGT

Figure 3

Domain structure of ADAMTS-M and translated nucleic acid sequence. A) Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding motif (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). **B)** ADAMTS-M nucleotide sequence with translated amino acid sequence above.

A



B

```
+1  P  G  R  P   T  R  P   K  A  P   S  H  S  A   P  L  L   G  L  A   L  L  R  M   H  Q  R
                                                                   Partial  Prodomain
    ================================================================================
25  CCGGGTCGAC CCACGCGTCC GAAGGCCCCC TCTCACTCCG CTCCACTCCT CGGGCTGGCT CTCCTGAGGA TGCACCAGCG
    GGCCCAGCTG GGTGCGCAGG CTTCCGGGGG AGAGTGAGGC GAGGTGAGGA GCCCGACCGA GAGGACTCCT ACGTGGTCGC

+1  H  P  R   A  R  C  P   P  L  C   V  A  G   I  L  A  C   G  F  L   L  G  C   W  G  P
                                                             Partial  Prodomain
    ================================================================================
105 TCACCCCCGG GCAAGATGCC CTCCCCTCTG TGTGGCCGGA ATCCTTGCCT GTGGCTTTCT CCTGGGCTGC TGGGGACCCT
    AGTGGGGGCC CGTTCTACGG GAGGGGAGAC ACACCGGCCT TAGGAACGGA CACCGAAAGA GGACCCGACG ACCCCTGGGA

+1  S  H  F  Q   Q  S  C   L  Q  A  L   E  P  Q   A  V  S   S  Y  L  S   P  G  A   P  L  K
    Partial  Prodomain
    ================================================================================
185 CCCATTTCCA GCAGAGTTGT CTTCAGGCTT TGGAGCCACA GGCCGTGTCT TCTTACTTGA GCCCTGGTGC TCCCTTAAAA
    GGGTAAAGGT CGTCTCAACA GAAGTCCGAA ACCTCGGTGT CCGGCACAGA AGAATGAACT CGGGACCACG AGGGAATTTT

+1  G  R  P  P   S  P  G   F  Q  R   Q  R  Q  R   Q  R  R   A  A  G   G  I  L  H   L  E  L
                                    Furin Cleavage  Site  (Motif)
                                            ==============
    Partial  Prodomain                                      Metalloproteinase  Domain
    ================================================================================
265 GGCCGCCCTC CTTCCCCTGG CTTCCAGAGG CAGAGGCAGA GGCAGAGGCG GGCTGCAGGC GGCATCCTAC ACCTGGAGCT
    CCGGCGGGAG GAAGGGGACC GAAGGTCTCC GTCTCCGTCT CCGTCTCCGC CCGACGTCCG CCGTAGGATG TGGACCTCGA

+1  L  V  A   V  G  P  D   V  F  Q   A  H  Q   E  D  T  E   R  Y  V   L  T  N   L  N  I
                                                            Metalloproteinase  Domain
    ================================================================================
345 GCTGGTGGCC GTGGGCCCCG ATGTCTTCCA GGCTCACCAG GAGGACACAG AGCGCTATGT GCTCACCAAC CTCAACATCG
    CGACCACCGG CACCCGGGGC TACAGAAGGT CCGAGTGGTC CTCCTGTGTC TCGCGATACA CGAGTGGTTG GAGTTGTAGC
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+1 G  A  E  L  L  R  D  P  S  L  G  A  Q  F  R  V  H  L  V  K  M  V  I  L  T  E  P
                                                     Metalloproteinase    Domain
   ================================================================================
425 GGGCAGAACT GCTTCGGGAC CCGTCCCTGG GGGCTCAGTT TCGGGTGCAC CTGGTGAAGA TGGTCATTCT GACAGAGCCT
    CCCGTCTTGA CGAAGCCCTG GGCAGGGACC CCCGAGTCAA AGCCCACGTG GACCACTTCT ACCAGTAAGA CTGTCTCGGA

+1  E  G  A  P  N  I  T  A  N  L  T  S  S  L  L  S  V  C  G  W  S  Q  T  I  N  P  E
                                                     Metalloproteinase    Domain
   ================================================================================
505 GAGGGTGCTC CAAATATCAC AGCCAACCTC ACCTCGTCCC TGCTGAGCGT CTGTGGGTGG AGCCAGACCA TCAACCCTGA
    CTCCCACGAG GTTTATAGTG TCGGTTGGAG TGGAGCAGGG ACGACTCGCA GACACCCACC TCGGTCTGGT AGTTGGGACT

+1  D  D  T  D  P  G  H  A  D  L  V  L  Y  I  T  R  F  D  L  E  L  P  D  G  N  R
                                       Metalloproteinase   Domain
   ================================================================================
585 GGACGACACG GATCCTGGCC ATGCTGACCT GGTCCTCTAT ATCACTAGGT TTGACCTGGA GTTGCCTGAT GGTAACCGGC
    CCTGCTGTGC CTAGGACCGG TACGACTGGA CCAGGAGATA TAGTGATCCA AACTGGACCT CAACGGACTA CCATTGGCCG

+1 Q  V  R  G  V  T  Q  L  G  G  A  C  S  P  T  W  S  C  L  I  T  E  D  T  G  F  D
   Metalloproteinase   Domain
   ================================================================================
665 AGGTGCGGGG CGTCACCCAG CTGGGCGGTG CCTGCTCCCC AACCTGGAGC TGCCTCATTA CCGAGGACAC TGGCTTCGAC
    TCCACGCCCC GCAGTGGGTC GACCCGCCAC GGACGAGGGG TTGGACCTCG ACGGAGTAAT GGCTCCTGTG ACCGAAGCTG

+1  L  G  V  T  I  A  H  E  I  G  H  S  F  G  L  E  H  D  G  A  P  G  S  G  C  G  P
                                             Zinc-binding   Motif
                          =====================================================
   Metalloproteinase   Domain
   ================================================================================
745 CTGGGAGTCA CCATTGCCCA TGAGATTGGG CACAGCTTCG GCCTGGAGCA CGACGGCGCG CCCGGCAGCG GCTGCGGCCC
    GACCCTCAGT GGTAACGGGT ACTCTAACCC GTGTCGAAGC CGGACCTCGT GCTGCCGCGC GGGCCGTCGC CGACGCCGGG

+1  S  G  H  V  M  A  S  D  G  A  A  P  R  A  G  L  A  W  S  P  C  S  R  R  Q  L
   Zinc-binding  Motif
   ================
   Metalloproteinase   Domain
   ================================================================================
825 CAGCGGACAC GTGATGGCTT CGGACGGCGC CGCGCCCCGC GCCGGCCTCG CCTGGTCCCC CTGCAGCCGC CGGCAGCTGC
    GTCGCCTGTG CACTACCGAA GCCTGCCGCG GCGCGGGGCG CGGCCGGAGC GGACCAGGGG GACGTCGGCG GCCGTCGACG

+1 L  S  L  L  S  A  G  R  A  R  C  V  W  D  P  P  R  P  Q  P  G  S  A  G  H  P  P
   Metalloproteinase   Domain
   =====================================================
905 TGAGCCTGCT CAGCGCAGGA CGGGCGCGCT GCGTGTGGGA CCCGCCGCGG CCTCAACCCG GGTCCGCGGG GCACCCGCCG
    ACTCGGACGA GTCGCGTCCT GCCCGCGCGA CGCACACCCT GGGCGGCGCC GGAGTTGGGC CCAGGCGCCC CGTGGGCGGC

+1  D  A  Q  P  G  L  Y  Y  S  A  N  E  Q  C  R  V  A  F  G  P  K  A  V  A  C  T  F
                                                          Disintegrin   Domain
            ======================================================================
985 GATGCGCAGC CTGGCCTCTA CTACAGCGCC AACGAGCAGT GCCGCGTGGC CTTCGGCCCC AAGGCTGTCG CCTGCACCTT
    CTACGCGTCG GACCGGAGAT GATGTCGCGG TTGCTCGTCA CGGCGCACCG GAAGCCGGGG TTCCGACAGC GGACGTGGAA
```

```
 +1  A R E  H L D M  C Q A  L S C  H T D P  L D Q  S S C  S R L
                        Disintegrin  Domain
     ==========================================================================
1065 CGCCAGGGAG CACCTGGATA TGTGCCAGGC CCTCTCCTGC CACACAGACC CGCTGGACCA AAGCAGCTGC AGCCGCCTCC
     GCGGTCCCTC GTGGACCTAT ACACGGTCCG GGAGAGGACG GTGTGTCTGG GCGACCTGGT TTCGTCGACG TCGGCGGAGG

 +1 L V P L  L D G  T E C G  V E K  W C S  K G R C  R S L  V E L
    Disintegrin  Domain
     ============================================================
1145 TCGTTCCTCT CCTGGATGGG ACAGAATGTG GCGTGGAGAA GTGGTGCTCC AAGGGTCGCT GCCGCTCCCT GGTGGAGCTG
     AGCAAGGAGA GGACCTACCC TGTCTTACAC CGCACCTCTT CACCACGAGG TTCCCAGCGA CGGCGAGGGA CCACCTCGAC

 +1  T P I A  A V H  G R W  S S W G  P R S  P C S  R S C G  G G V
                                              Heparin-binding  Motif
                                               ====================
                                                  Thrombospondin   Submotif
                               ==============================================
1225 ACCCCCATAG CAGCAGTGCA TGGGCGCTGG TCTAGCTGGG GTCCCCGAAG TCCTTGCTCC CGCTCCTGCG GAGGAGGTGT
     TGGGGGTATC GTCGTCACGT ACCCGCGACC AGATCGACCC CAGGGGCTTC AGGAACGAGG GCGAGGACGC CTCCTCCACA

 +1  V T R  R R Q C  N N P  R P A  F G G R  A C V  G A D  L Q A
                           Thrombospondin  Submotif
     ==========================================================================
1305 GGTCACCAGG AGGCGGCAGT GCAACAACCC CAGACCTGCC TTTGGGGGGC GTGCATGTGT TGGTGCTGAC CTCCAGGCCG
     CCAGTGGTCC TCCGCCGTCA CGTTGTTGGG GTCTGGACGG AAACCCCCCG CACGTACACA ACCACGACTG GAGGTCCGGC

 +1 E M C N  T Q A  C E K T  Q L E  F M S  Q Q C A  R T D  G Q P
    Thrombospondin  Submotif
     ======================================================
1385 AGATGTGCAA CACTCAGGCC TGCGAGAAGA CCCAGCTGGA GTTCATGTCG CAACAGTGCG CCAGGACCGA CGGCCAGCCG
     TCTACACGTT GTGAGTCCGG ACGCTCTTCT GGGTCGACCT CAAGTACAGC GTTGTCACGC GGTCCTGGCT GCCGGTCGGC

 +1  L R S S  P G G  A S F  Y H W G  A A V  P H S  Q G D A  L C R
1465 CTGCGCTCCT CCCCTGGCGG CGCCTCCTTC TACCACTGGG GTGCTGCTGT ACCACACAGC CAAGGGGATG CTCTGTGCAG
     GACGCGAGGA GGGGACCGCC GCGGAGGAAG ATGGTGACCC CACGACGACA TGGTGTGTCG GTTCCCCTAC GAGACACGTC

 +1  H M C  R A I G  E S F  I M K  R G D S  F L D  G T R  C M P
1545 ACACATGTGC CGGGCCATTG GCGAGAGCTT CATCATGAAG CGTGGAGACA GCTTCCTCGA TGGGACCCGG TGTATGCCAA
     TGTGTACACG GCCCGGTAAC CGCTCTCGAA GTAGTACTTC GCACCTCTGT CGAAGGAGCT ACCCTGGGCC ACATACGGTT

 +1 S G P R  E D G  T L S L  C V S  G S C  R T F G  C D G  R M D
1625 GTGGCCCCCG GGAGGACGGG ACCCTGAGCC TGTGTGTGTC GGGCAGCTGC AGGACATTTG GCTGTGATGG TAGGATGGAC
     CACCGGGGGC CCTCCTGCCC TGGGACTCGG ACACACACAG CCCGTCGACG TCCTGTAAAC CGACACTACC ATCCTACCTG

 +1  S Q Q V  W D R  C Q V  C G G D  N S T  C S P  R K G S  F T A
1705 TCCCAGCAGG TATGGGACAG GTGCCAGGTG TGTGGTGGGG ACAACAGCAC GTGCAGCCCA CGGAAGGGCT CTTTCACAGC
     AGGGTCGTCC ATACCCTGTC CACGGTCCAC ACACCACCCC TGTTGTCGTG CACGTCGGGT GCCTTCCCGA GAAAGTGTCG

 +1  G R A  R E Y V  T F L  T V T  P N L T  S V Y  I A N  H R P
1785 TGGCAGAGCG AGAGAATATG TCACGTTTCT GACAGTTACC CCCAACCTGA CCAGTGTCTA CATTGCCAAC CACAGGCCTC
     ACCGTCTCGC TCTCTTATAC AGTGCAAAGA CTGTCAATGG GGGTTGGACT GGTCACAGAT GTAACGGTTG GTGTCCGGAG
```

+1 L F T H L A V R I G G R Y V V A G K M S I S P N T T Y
1865 TCTTCACACA CTTGGCGGTG AGGATCGGAG GGCGCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCCTAA CACCACCTAC
AGAAGTGTGT GAACCGCCAC TCCTAGCCTC CCGCGATACA GCACCGACCC TTCTACTCGT AGAGGGGATT GTGGTGGATG

+1 P S L L E D G R V E Y R V A L T E D R L P R L E E I R
1945 CCCTCCCTCC TGGAGGATGG TCGTGTCGAG TACAGAGTGG CCCTCACCGA GGACCGGCTG CCCCGCCTGG AGGAGATCCG
GGGAGGGAGG ACCTCCTACC AGCACAGCTC ATGTCTCACC GGGAGTGGCT CCTGGCCGAC GGGGCGGACC TCCTCTAGGC

+1 I W G P L Q E D A D I Q V Y R R Y G E E Y G N L T R
2025 CATCTGGGGA CCCCTCCAGG AAGATGCTGA CATCCAGGTT TACAGGCGGT ATGGCGAGGA GTATGGCAAC CTCACCCGCC
GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCCA TACCGCTCCT CATACCGTTG GAGTGGGCGG

+1 P D I T F T Y F Q P K P R Q A W V W A A V R G P C S V
2105 CAGACATCAC CTTCACCTAC TTCCAGCCTA AGCCACGGCA GGCCTGGGTG TGGGCCGCTG TGCGTGGGCC CTGCTCGGTG
GTCTGTAGTG GAAGTGGATG AAGGTCGGAT TCGGTGCCGT CCGGACCCAC ACCCGGCGAC ACGCACCCGG GACGAGCCAC

+1 S C G A G L R W V N Y S C L D Q A R K E L V E T V Q C
2185 AGCTGTGGGG CAGGGCTGCG CTGGGTAAAC TACAGCTGCC TGGACCAGGC CAGGAAGGAG TTGGTGGAGA CTGTCCAGTG
TCGACACCCC GTCCCGACGC GACCCATTTG ATGTCGACGG ACCTGGTCCG GTCCTTCCTC AACCACCTCT GACAGGTCAC

+1 Q G S Q Q P P A W P E A C V L E P C P P Y W A V G D
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCCTGC GTGCTCGAAC CCTGCCCTCC CTACTGGGCG GTGGGAGACT
GGTTCCCTCG GTCGTCGGTG GTCGCACCGG TCTCCGGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCCTCTGA

+1 F G P C S A S C G G G L R E R P V R C V E A Q G S L L
2345 TCGGCCCATG CAGCGCCTCC TGTGGGGGTG GCCTGCGGGA GCGGCCAGTG CGCTGCGTGG AGGCCCAGGG CAGCCTCCTG
AGCCGGGTAC GTCGCGGAGG ACACCCCCAC CGGACGCCCT CGCCGGTCAC GCGACGCACC TCCGGGTCCC GTCGGAGGAC

+1 K T L P P A R C R A G A Q Q P A V A L E T C N P Q P C
2425 AAGACATTGC CCCCAGCCCG GTGCAGAGCA GGGGCCCAGC AGCCAGCTGT GGCGCTGGAA ACCTGCAACC CCCAGCCCTG
TTCTGTAACG GGGGTCGGGC CACGTCTCGT CCCCGGGTCG TCGGTCGACA CCGCGACCTT TGGACGTTGG GGGTCGGGAC

+1 P A R W E V S E P S S C T S A G G A G L A L E N E T
2505 CCCTGCCAGG TGGGAGGTGT CAGAGCCCAG CTCATGCACA TCAGCTGGTG GAGCAGGCCT GGCCTTGGAG AACGAGACCT
GGGACGGTCC ACCCTCCACA GTCTCGGGTC GAGTACGTGT AGTCGACCAC CTCGTCCGGA CCGGAACCTC TTGCTCTGGA

+1 C V P G A D G L E A P V T E G P G S V D E K L P A P E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTGACTGA GGGGCCTGGC TCCGTAGATG AGAAGCTGCC TGCCCCTGAG
CACACGGTCC CCGTCTACCG GACCTCCGAG GTCACTGACT CCCCGGACCG AGGCATCTAC TCTTCGACGG ACGGGGACTC

+1 P C V G M S C P P G W G H L D A T S A G E K A P S P W
2665 CCCTGTGTCG GGATGTCATG TCCTCCAGGC TGGGGCCATC TGGATGCCAC CTCTGCAGGG GAGAAGGCTC CCTCCCCATG
GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCCGGTAG ACCTACGGTG GAGACGTCCC CTCTTCCGAG GGAGGGGTAC

+1 G S I R T G A Q A A H V W T P A A G S C S V S C G R
2745 GGGCAGCATC AGGACGGGGG CTCAAGCTGC ACACGTGTGG ACCCCTGCGG CAGGGTCGTG CTCCGTCTCC TGCGGGCGAG
CCCGTCGTAG TCCTGCCCCC GAGTTCGACG TGTGCACACC TGGGGACGCC GTCCCAGCAC GAGGCAGAGG ACGCCCGCTC

+1 G L M E L R F L C M D S A L R V P V Q E E L C G L A S
2825 GTCTGATGGA GCTGCGTTTC CTGTGCATGG ACTCTGCCCT CAGGGTGCCT GTCCAGGAAG AGCTGTGTGG CCTGGCAAGC
CAGACTACCT CGACGCAAAG GACACGTACC TGAGACGGGA GTCCCACGGA CAGGTCCTTC TCGACACACC GGACCGTTCG

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   +1  K  P  G  S  R  R  E  V  C  Q  A  V  P  C  P  A  R  W  Q  Y  K  L  A  A  C  S  V
2905  AAGCCTGGGA GCCGGCGGGA GGTCTGCCAG GCTGTCCCGT GCCCTGCTCG GTGGCAGTAC AAGCTGGCGG CCTGCAGCGT
      TTCGGACCCT CGGCCGCCCT CCAGACGGTC CGACAGGGCA CGGGACGAGC CACCGTCATG TTCGACCGCC GGACGTCGCA

   +1  S  C  G  R  G  V  V  R  R  I  L  Y  C  A  R  A  H  G  E  D  D  G  E  E  I  L
2985  GAGCTGTGGG AGAGGGGTCG TGCGGAGGAT CCTGTATTGT GCCCGGGCCC ATGGGGAGGA CGATGGTGAG GAGATCCTGT
      CTCGACACCC TCTCCCCAGC ACGCCTCCTA GGACATAACA CGGGCCCGGG TACCCCTCCT GCTACCACTC CTCTAGGACA

   +1  L  D  T  Q  C  Q  G  L  P  R  P  E  P  Q  E  A  C  S  L  E  P  C  P  P  R  W  K
3065  TGGACACCCA GTGCCAGGGG CTGCCTCGCC CGGAACCCCA GGAGGCCTGC AGCCTGGAGC CCTGCCCACC TAGGTGGAAA
      ACCTGTGGGT CACGGTCCCC GACGGAGCGG GCCTTGGGGT CCTCCGGACG TCGGACCTCG GGACGGGTGG ATCCACCTTT

   +1  V  M  S  L  G  P  C  S  A  S  C  G  L  G  T  A  R  R  S  V  A  C  V  Q  L  D  Q
3145  GTCATGTCCC TTGGCCCATG TTCGGCCAGC TGTGGCCTTG GCACTGCTAG ACGCTCGGTG GCCTGTGTGC AGCTCGACCA
      CAGTACAGGG AACCGGGTAC AAGCCGGTCG ACACCGGAAC CGTGACGATC TGCGAGCCAC CGGACACACG TCGAGCTGGT

   +1  G  Q  D  V  E  V  D  E  A  A  C  A  A  L  V  R  P  E  A  S  V  P  C  L  I  A
3225  AGGCCAGGAC GTGGAGGTGG ACGAGGCGGC CTGTGCGGCG CTGGTGCGGC CCGAGGCCAG TGTCCCCTGT CTCATTGCCG
      TCCGGTCCTG CACCTCCACC TGCTCCGCCG GACACGCCGC GACCACGCCG GGCTCCGGTC ACAGGGGACA GAGTAACGGC

   +1  D  C  T  Y  R  W  H  V  G  T  W  M  E  C  S  V  S  C  G  D  G  I  Q  R  R  R  D
                                                          Thrombospondin  Submotif
                                  ================================================================
3305  ACTGCACCTA CCGCTGGCAT GTTGGCACCT GGATGGAGTG CTCTGTTTCC TGTGGGGATG GCATCCAGCG CCGGCGTGAC
      TGACGTGGAT GGCGACCGTA CAACCGTGGA CCTACCTCAC GAGACAAAGG ACACCCCTAC CGTAGGTCGC GGCCGCACTG

   +1  T  C  L  G  P  Q  A  Q  A  P  V  P  A  D  F  C  Q  H  L  P  K  P  V  T  V  R  G
                  Thrombospondin  Submotif
      ============================================================================================
3385  ACCTGCCTCG GACCCCAGGC CCAGGCGCCT GTGCCAGCTG ATTTCTGCCA GCACTTGCCC AAGCCGGTGA CTGTGCGTGG
      TGGACGGAGC CTGGGGTCCG GGTCCGCGGA CACGGTCGAC TAAAGACGGT CGTGAACGGG TTCGGCCACT GACACGCACC

   +1  C  W  A  G  P  C  V  G  Q  G  T  P  S  L  V  P  H  E  E  A  A  A  P  G  R  T
      Thrombospondin  Submotif
      ==============================
3465  CTGCTGGGCT GGGCCCTGTG TGGGACAGGG TACGCCCAGC CTGGTGCCCC ACGAAGAAGC CGCTGCTCCA GGACGGACCA
      GACGACCCGA CCCGGGACAC ACCCTGTCCC ATGCGGGTCG GACCACGGGG TGCTTCTTCG GCGACGAGGT CCTGCCTGGT

   +1  T  A  T  P  A  G  A  C  G  R  Q  H  L  E  P  T  G  T  I  D  M  R  G  P  G  Q  A
3545  CAGCCACCCC TGCTGGTGCC TGTGGCAGGC AGCACCTTGA GCCAACAGGA ACCATTGACA TGCGAGGCCC AGGGCAGGCA
      GTCGGTGGGG ACGACCACGG ACACCGTCCG TCGTGGAACT CGGTTGTCCT TGGTAACTGT ACGCTCCGGG TCCCGTCCGT

   +1  D  C  A  V  A  I  G  R  P  L  G  E  V  V  T  L  R  V  L  E  S  S  L  N  C  S  A
3625  GACTGTGCAG TGGCCATTGG GCGGCCCCTC GGGGAGGTGG TGACCCTCCG CGTCCTTGAG AGTTCTCTCA ACTGCAGTGC
      CTGACACGTC ACCGGTAACC CGCCGGGGAG CCCCTCCACC ACTGGGAGGC GCAGGAACTC TCAAGAGAGT TGACGTCACG

   +1  G  D  M  L  L  L  W  G  R  L  T  W  R  K  M  C  R  K  L  L  D  M  T  F  S  S
3705  GGGGGACATG TTGCTGCTTT GGGGCCGGCT CACCTGGAGG AAGATGTGCA GGAAGCTGTT GGACATGACT TTCAGCTCCA
      CCCCCTGTAC AACGACGAAA CCCCGGCCGA GTGGACCTCC TTCTACACGT CCTTCGACAA CCTGTACTGA AAGTCGAGGT

   +1  K  T  N  T  L  V  V  R  Q  R  C  G  R  P  G  G  G  V  L  L  R  Y  G  S  Q  L  A
3785  AGACCAACAC GCTGGTGGTG AGGCAGCGCT GCGGGCGGCC AGGAGGTGGG GTGCTGCTGC GGTATGGGAG CCAGCTTGCT
      TCTGGTTGTG CGACCACCAC TCCGTCGCGA CGCCCGCCGG TCCTCCACCC CACGACGACG CCATACCCTC GGTCGAACGA
```

```
+1    P  E  T  F  Y  R  E  C  D  M  Q  L  F  G  P  W  G  E  I  V  S  P  S  L  S  P  A
3865  CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTTG GGCCCTGGGG TGAAATCGTG AGCCCCTCGC TGAGTCCAGC
      GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAAC CCGGGACCCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTCG

+1    T  S  N  A  G  G  C  R  L  F  I  N  V  A  P  H  A  R  I  A  I  H  A  L  A  T
3945  CACGAGTAAT GCAGGGGGCT GCCGGCTCTT CATTAATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
      GTGCTCATTA CGTCCCCCGA CGGCCGAGAA GTAATTACAC CGAGGCGTGC GTGCCTAACG GTAGGTACGG GACCGGTGGT

+1    N  M  G  A  G  T  E  G  A  N  A  S  Y  I  L  I  R  D  T  H  S  L  R  T  T  A  F
4025  ACATGGGCGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCCGG GACACCCACA GCTTGAGGAC CACAGCGTTC
      TGTACCCGCG ACCCTGGCTC CCTCGGTTAC GGTCGATGTA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTCGCAAG

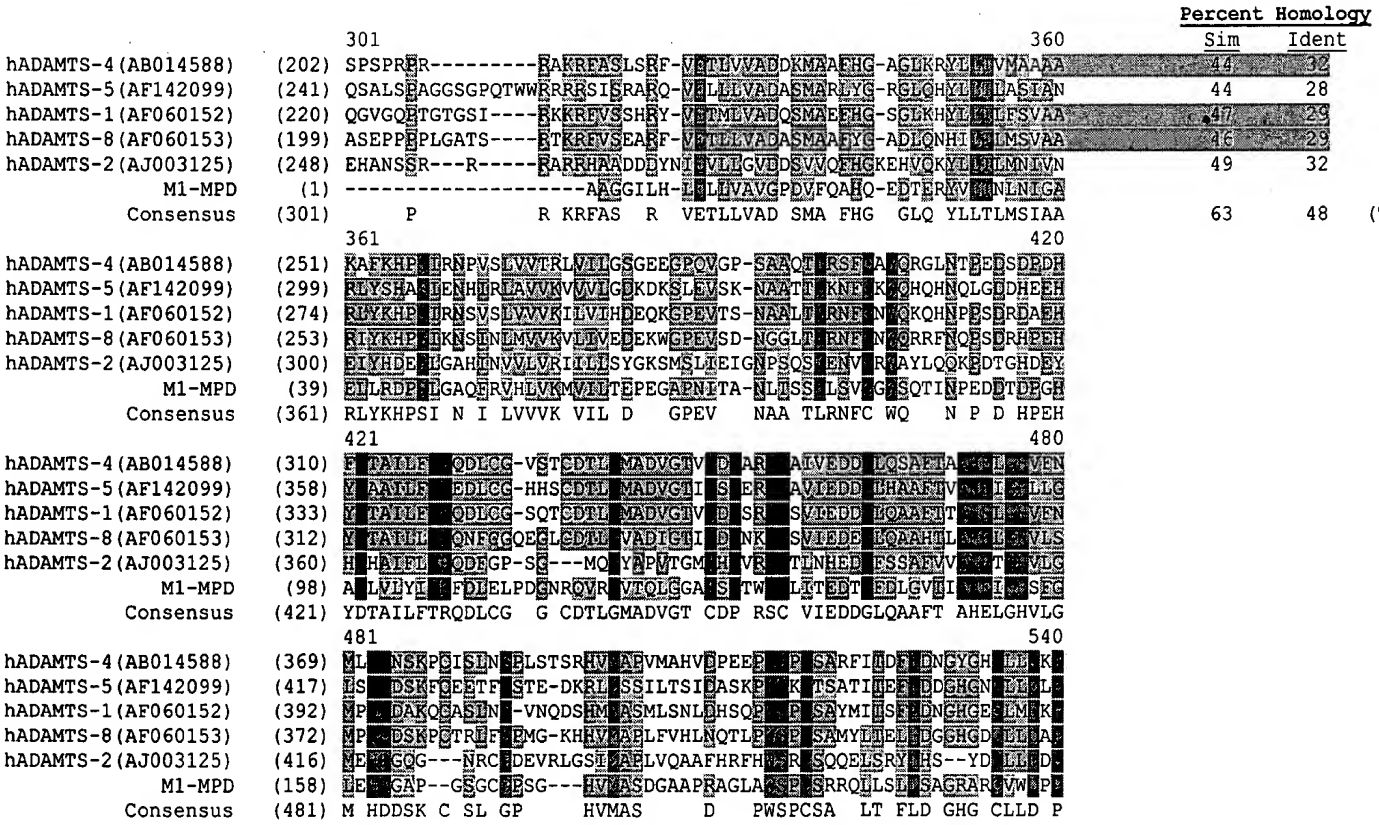
+1    H  G  Q  Q  V  L  Y  W  E  S  E  S  S  Q  A  E  M  E  F  S  E  G  F  L  K  A  Q
4105  CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTTCAGC GAGGGCTTCC TGAAGGCTCA
      GTACCCGTCG TCCACGAGAT GACCCTCAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT

+1    A  S  L  R  G  Q  Y  W  T  L  Q  S  W  V  P  E  M  Q  D  P  Q  S  W  K  G  K
4185  GGCCAGCCTG CGGGGCCAGT ACTGGACCCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCCTGG AAGGGAAAGG
      CCGGTCGGAC GCCCCGGTCA TGACCTGGGA GGTTAGTACC CATGGCCTCT ACGTCCTGGG AGTCAGGACC TTCCCTTTCC

+1    E  G  T
4265  AAGGAACC
      TTCCTTGG
```

Fig. 4

Metalloproteinase Domain Alignment of ADAMTS-M v. ADAMTS Family



```
                                541                                                        600
hADAMTS-4(AB014588)    (429)  EAP--LHLPVTFPG--KDYDADRQCQLTFGPDSRHCP--QLPPPCAALWCSGHLNGHAMC
hADAMTS-5(AF142099)    (476)  RKQ--ILGPEELPG--QTYDATQQCNLTFGPEYSVCP---GMDVCARLWCAVVRQGQMVC
hADAMTS-1(AF060152)    (451)  QNP--IQLPGDLPG--TSYDANRQCQFTFGEDSKHCP--DAASTCSTLWCTGTSGGVLVC
hADAMTS-8(AF060153)    (431)  GAA--LPLPTGLPGRMALYQLDQQCRQIFGPDFRHCPNTSAQDVCAQLWCH-TDGAEPLC
hADAMTS-2(AJ003125)    (471)  FAHDWPALP-QLPG--LHYSMNEQCRFDFGLGYMMCTAFRTFDPCKQLWCS-HPDNPYFC
             M1-MPD    (213)  RP----------------------------------------------------------
          Consensus    (541)  A     LP  LPG    YDA  QC  TFGPD  HCP      D CA LWC     G   C
```